## REMARKS

Claims 1, 3-14, 44, and 59-70, as amended, are pending in this application for the Examiner's review and consideration. Independent claim 1 was amended to recite that the injectable composition "when administered to an animal, forms a depot that" releases the active compound over time (Specification at ¶¶ [0030] and [0034]. Independent claim 44 was amended to recite that the solution "when injected into water, forms a cohesive oily mass" (*Id.* at ¶ [0011]. Claims 1 and 44 were also amended to more clearly recite that the salt includes both the pharmacologically active compound and the lipophilic counterion in response to the Examiner's assertion, at page 9 of the Office Action, that the phrase "a salt formed of the pharmacologically active compound and a lipophilic counterion; and a pharmaceutically acceptable, water immiscible solvent" was unclear. Claims 9, 13, 65, and 69 were amended to simply be written in independent form. No new matter is added by these claim amendments so that their entry at this time is warranted.

### THE REJECTIONS UNDER 35 U.S.C. § 103(A)

Claims 1, 3-8, 11, 12, 14, 44, 59-64, 67, 68, and 70 were rejected under 35 U.S.C. § 103(a) as obvious over U.S. Patent No. 6,309,663 to Patel *et al.* ("Patel") for the reasons set forth on pages 2-3 of the Office Action. Specifically, the Examiner asserts "Patel et al. teach a pharmaceutical composition for oral or parenteral use [ ] comprising an active agent, such as gentamycin (antibiotic) and fluoxetine [ ], combined with a hydrophobic surfactant (water immiscible solvent) such as castor oil, palm kernel oil, and corn oil [ ] and ionizable surfactants that are in their ionized form [ ] such as oleic acid, capric acid (decanoic acid), linoleic acid, and lauric acid [ ]" (Office Action at page 3). The Examiner goes on to state that "the prior art teaches the identical chemical structure" and asserts that "the properties applicant discloses and/or claims (i.e., the release of the active compound over time) are necessarily present" (*Id.*). Therefore, the Examiner concludes "it would have been obvious to one of ordinary skill in the art at the time it was made to combine an active agent such as gentamycin and fluoxetine [ ] with a water immiscible solvent such as castor oil, palm kernel oil, and corn oil [ ] and ionizable surfactants that are in their ionized form [ ] such as oleic acid, capric acid (decanoic acid), linoleic acid, and lauric acid [ ] motivated by the teaching of Patel et al. that the composition is a

successful carrier for oral or injectable agents" (*Id.*). Applicants respectfully traverses.

As the Examiner is aware, in order to render claims obvious under 35 U.S.C. § 103(a), the prior art must disclose or suggest every limitation of the claimed invention and provide the person of skill in the art with a reasonable expectation that the invention will work for its intended purpose. *KSR International Co. v. Teleflex Inc. et al.*, 127 S.Ct. 1727 at 1739-41 (2007). Applicant respectfully submits that Patel does not render obvious the claims, as amended, because Patel does not disclose or suggest every limitation recited in the claims, as amended, or provide a reasonable expectation that the invention will work for its intended purpose.

Patel discloses a triglyceride free pharmaceutical system having a dosage form of an absorption enhancing composition comprising at least two surfactants, at least one of which is hydrophilic, and a hydrophobic therapeutic agent (Patel, column 4, lines 1-5).

Patel, however, does not disclose each and every feature of the invention recited in independent claims 1 and 44, as amended, suggest the invention, or provide a reasonable expectation of success. For example, Patel does not disclose or suggest forming a salt comprising a pharmacologically active compound and a lipophilic counterion or to combine the resulting salt with a water immiscible solvent. Patel also does not disclose a composition that "when administered to an animal forms a depot that releases the active compound over time" (independent claim 1) or the feature that the composition "when injected into water, forms a cohesive oily mass" (independent claim 44). Indeed, as discussed below Patel teaches away from such a composition.

The Examiner asserts that Patel discloses gentamycin and fluoxetine as a pharmacologically active compound. Similarly, the Examiner asserts that Patel discloses ionizable surfactants that are in their ionized form, such as oleic acid, capric acid, linoleic acid, and lauric acid and hydrophobic surfactants (water immiscible solvent) such as castor oil, palm kernel oil, and corn oil. Each of these components, however, is simply included as part of a long laundry list of active compounds. For example, gentamycin and fluoxetine are included in a list of pharmacologically active compounds that spans 3 columns of the patent (*Id.* at column 29, line 41 to column 32, line 18). Indeed, many of the disclosed pharmacologically active

compounds are not basic or acidic and, thus, are not even capable of forming a salt, as required by independent claims 1 and 44. Similarly, the disclosure of surfactants is part of a long laundry list of surfactants spanning over 10 pages of the patent (*Id.* at column 6, line 55 to column 29 line 5).

There is, however, no disclosure or suggestion in Patel that would motivate one of ordinary skill in the art to select, from the long laundry list of pharmacologically active compounds recited therein, a pharmacologically active compound that can form a salt with a lipophilic counterion; to select, from the long laundry list of surfactants disclosed therein, a surfactant that is a lipophilic counterion; to then form a salt between the pharmacologically active compound and the lipophilic counterion; and to then combine the resulting salt with a water immiscible solvent. Indeed, Patel provides as much motivation to choose a pharmacologically active compound and a hydrophilic surfactant that *cannot* form a salt with each other (for example, a pharmacologically active compound such as cromalyn sodium, mannitol, or oxytocin (disclosed in Patel at column 30, lines 25, 48 and 55, respectively) combined with a hydrophilic surfactant such as sodium oleate or sodium cholate (disclosed in Patel at column 22, lines 23 and 25, respectively)). Such a combination would not result in the composition recited in independent claims 1 and 44. Patel is a vast disclosure and there is no motivation or suggestion to select the combination of components required to arrive at Applicants invention. Indeed, combining "an active agent such as gentamycin [or] fluoxetine [ ] and ionizable surfactant that are in their ionized form [ ] such as oleic acid, capric acid (decanoic acid), linoleic acid, and lauric acid [ ]," as the Examiner asserts would be obvious to do (Office Action at page 3), would not result in "a salt formed of the pharmacologically active compound and a lipophilic counterion," as required by independent claims 1 and 44, as amended. Thus, even the Examiner's reading of Patel would not arrive at the claimed compositions.

Furthermore, not only does Patel provide no suggestion or motivation to select a pharmacologically active compound that can form a salt with a lipophilic counterion; to select a surfactant that is a lipophilic counterion; to then form a salt between the pharmacologically active compound and the lipophilic counterion; and to then combine the resulting salt with a water immiscible solvent, Patel does not disclose or suggest the feature recited in independent claim 1, as amended, that the composition "when administered to an animal forms a *depot that*

*releases the active compound over time*" or the feature, recited in independent claim 44, as amended, that the composition "when injected into water, forms a cohesive oily mass."

First, Patel does not disclose the formation of a depot, which is defined in the specification as "a cohesive oily mass" (Specification at ¶ [0030] and [0034]). Rather, Patel discloses that when the compositions disclosed therein when "mixed with an aqueous diluent either in vitro or in vivo, form aqueous dispersions having *very small particle size*" (*Id.* at column 4, lines 50-54, emphasis added; *see also*, column 4, lines 1-23 and column 44, line 45 to column 45, line 24). Indeed, Patel states that the particle size is "much smaller than the larger particles characteristic of vesicular, emulsion or microemulsion phases" (*Id.* at column 45, lines 12-15) and that when the compositions are diluted "the components of the absorption enhancing composition remain solubilized and thus do not suffer the problems of precipitation or agglomeration in the time frame relevant for absorption" (*Id.* at column 45, lines 51-55). Clearly, the aqueous dispersions having *very small particle size* disclosed in Patel are not a depot (*i.e.*, a *cohesive* oily mass), as required by independent claims 1 and 44.

Furthermore, not only does Patel not disclose the formation of a depot, Patel does not disclose a composition that "releases the active compound over time," as recited in independent claim 1. Rather, Patel discloses "an absorption enhancing composition" (*Id.* at column 4, lines 1-5 and column 45, lines 51-58) that "enhances the rate, extent, and/or consistency of bioabsorption of the active agent" (*Id.* at column 4, lines 57-58, *see also* column 35, lines 25-28 disclosing that "the composition includes sufficient amounts of the absorption enhancing components [*i.e.*, the surfactants] to provide a therapeutically meaningful *increase* in the rate and/or extent of bioabsorption" (emphasis added)). Indeed, this enhanced absorption is because of the small particle size (*Id.* at column 4, lines 50-60)column 33, lines 45-62). Thus, Patel discloses "absorption enhancing compositions" that are contrary to the claimed depot forming compositions that "releases the active compound over time," as recited in independent claim 1.

Thus, the small particle, absorption enhancing compositions disclosed in Patel are completely different from the depot compositions recited in independent claims 1 and 44 that release an active compound over time. Indeed, Patel, by teaching compositions that "form aqueous dispersions having very small particle size" (*Id.* at column 4, lines 50-54) teaches away

from the composition recited in independent claims 1 and 44 that "when administered to an animal forms a depot" (claim 1) and "when injected into water, forms a cohesive oily mass" (claim 44). Similarly, Patel, by teaching "an absorption enhancing composition" (*Id.* at column 4, lines 1-5 and column 45, lines 51-58) that "enhances the rate, extent, and/or consistency of bioabsorption of the active agent (*Id.* at column 4, lines 57-58), teaches away from the composition recited in independent claim 1 that requires "release[ing] the active compound over time." The compositions recited in independent claims 1 and 44 are contrary to the teaching of Patel.

The Examiner, however, again asserts that:

> "Products of identical chemical composition [ ] cannot have mutually exclusive properties." A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims (i.e. the release of the active compound over time ) are necessarily present. In re Spada, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990).

(Office Action, page 3). The Manual of Patent Examining Procedure ("MPEP") states "'[w]hen the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing they are not'" (MPEP at ¶ 2112.01, *citing In re Spada*, 911 F.2d at 709, 15 USPQ2d at 1658) and goes on to state that "[t]herefore, the *prima facie* case can be rebutted by evidence showing that the prior art products do not necessarily posses the characteristics of the claimed product" ((MPEP at ¶ 2112.01, *citing In re Best*, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977)).

Initially, applicants note that formulations, even if they contain the same components, can have different properties depending on, for example, the amounts of each component of the composition, the ratio of components, and how the components are combined and processed.[1] Thus, even if there was motivation to select from the laundry list of components disclosed in Patel the components recited in independent claims 1 and 44 (which, for the reasons discussed above, there is not), the compositions would not necessarily have the same characteristics as the claimed composition.

Moreover, Applicant's have met the burden of showing that the claimed compositions do

[1] For example, although diamond, graphite, and coal are each the single element carbon, they have

not have the same characteristics as the prior art products, *i.e.*, Patel. Applicants have clearly demonstrated that the claimed compositions are different from those described in Patel. First, as discussed above, Patel clearly describes a composition that when "mixed with an aqueous diluent either in vitro or in vivo, form aqueous dispersions having *very small particle size*" (*Id.* at column 4, lines 50-54, emphasis added; *see also*, column 4, lines 1-23 and column 44, line 45 to column 45, line 24). In contrast, the claimed compositions form a depot or a cohesive oily mass when mixed with an aqueous diluent either in vitro or in vivo. The aqueous dispersions having *very small particle size* disclosed in Patel are clearly not a depot (*i.e.*, a *cohesive* oily mass), as required by independent claims 1 and 44. Second, as also discussed above, the compositions disclosed in Patel are "an absorption enhancing composition" (*Id.* at column 4, lines 1-5 and column 45, lines 51-58) that "enhances the rate, extent, and/or consistency of bioabsorption of the active agent" (*Id.* at column 4, lines 57-58) that "provide a therapeutically meaningful increase in the rate and/or extent of bioabsorption" (*Id.* at column 35, lines 25-28). In contrast, the claimed compositions "release[] the active compound over time." Indeed, Examples 7-9 of the application illustrate releasing the active compound over time. Considering the description in Patel of the compositions disclosed therein and considering the claimed compositions (as well as the disclosure in the specification of the above-identified matter, including the Examples) clearly establishes that the prior art products do not posses the characteristics of the claimed product.

The Examiner also asserts, with regard to the feature recited in claim 1 that the composition "releases the active compound over time," that

> fluoxetine as an elimination half life of 1 to 3 days. As such, the composition of Patel would be present in the body of the patient for at least 1 to 3 days with acute administration and 4 to 6 days with chronic administration.

(Office Action, page 10). That fluoxetine has an elimination half life of 1 to 3 days is not a teaching of a composition that "releases the active compound over time." Half life and release over time are completely different concepts. Half life is a measurement of the time a compound remains in the bloodstream *after* it has been released into the blood stream, *i.e.*, it measures a bodies ability to metabolize and/or excrete a compound. The phrase "releases the active compound over time," in contrast, is a measure of how fast the compound is released *into* the

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completely different properties.

blood stream after the dosage form is administered, *i.e.*, how fast it is released from the depot. This is clearly described in the specification, which states that the

> drug depot [ ] releases a pharmaceutically effective amount of the active compound over time. In one embodiment the pharmacologically active compound *is released over a period of 2 days or greater* and is present in the blood or tissue of the mammal at a pharmaceutically effective amount for that period. In other embodiments, the compound is released and present at a pharmaceutically effective amount over a period of 3 days or 4 days or 5 days or greater as described above.

(Specification at ¶ [0034], *see also* ¶¶ [0018], [0016], [0033], and Examples 7-8, ¶¶ [0059] - [0065]). Indeed, Example 7 of the specification clearly demonstrates that Applicants understood the concept of half-life and release rate and recognized that they are different concepts. One of ordinary skill in the art reading the specification would readily understand that the phrase "releases the active compound over time" means that the composition controls the release of the pharmacologically active compound from the depot so that the active compound is more slowly released into the blood stream, and to be completely different from, and unrelated to, the half-life of a compound, which relates to the rate of metabolism and/or excretion of a compound.

The rejection of the claims as obvious over Patel involves the impermissible use of hindsight to reconstruct Applicants' invention. Applicant's disclosure is being used as a blueprint to combine selected parts of Patel, when there is no motivation to do so, to arrive at Applicants' invention. It is well settled that hindsight cannot be used to reject a claim as obvious. *In re Sernaker,* 702 F.2d 989, 994 (Fed. Cir. 1983); *In re Rinehart, 531* F.2d 1048 (CCPA 1976); *In re Imperato,* 486 F.2d 585 (CCPA 1973); *In re Adams,* 356 F.2d 998 (CCPA 1966); *In re Anita Dembiczak,* 75 F.3d 994, 999 (Fed. Cir. 1999); *C.R. Bard Inc. v. M3 Systems, Inc.,* 157 F.3d 1340, 1352 (Fed. Cir. 1998) citing *Fromson v. Advance Offset Plate, Inc.,* 755 F.2d 1549, 1556 (Fed. Cir. 1985) (holding the prior art must suggest to one of ordinary skill in the art the desirability of the claimed combination). The Examiner is selectively picking and choosing various parts of the broad disclosure of Patel, absent a motivation to do so, to reconstruct Applicants' invention. Such hindsight reconstruction is impermissible as a matter of law.

Concerning hindsight reconstruction, the Examiner again repeats her assertion, set forth in the previous Office Action that

> It is not clear to the Examiner what picking and choosing is needed in order to determine

> what medicaments are specifically described in Patel et al. to determine which agents are included as part of the invention. *All that is needed to implement the disclosure of Patel et al.* is to combine any of the agents recited [ ] with the water immiscible solvents recited along with decanoic acid. There does not appear to be any difficulty in arriving at the decision of which agents to choose.

(Office Action, page a 11-2, emphasis added). The issue is not what "*is needed to implement the disclosure of Patel et al.*" The issue is what is needed to implement the *claimed invention* in view of Patel. As discussed above, to arrive at Applicants' invention, one must first select a pharmacologically active compound that can form a salt with a lipophilic counterion from the long laundry list of active compounds recited in Patel (many of which do not form a salt), must then select a surfactant that is a lipophilic counterion from the long list of surfactants disclosed in Patel (many of which are not lipophilic salts), must then form a salt between the pharmacologically active compound and the lipophilic counterion, and then combine the resulting salt with a water immiscible solvent. Again, Patel is a vast disclosure and there is no motivation or suggestion to select the specific combination of components required to arrive at Applicants invention. The Examiner has used Applicants specification as a road map to pick and choose selected disclosures in Patel to arrive at Applicants invention without any motivation to do so.

Furthermore, even of there was a motivation or suggestion to select the specific combination of components required to arrive at Applicants invention (which, for the reasons discussed above, there is not), there is no reasonable expectation that such a combination would provide a composition " that when administered to an animal, forms a depot that releases the active compound over time" (claim 1) or that "form a clear injectable solution that, when injected into water, forms a cohesive oily mass" (claim 44) because Patel teaches the opposite, *i.e.*, "small particles" and "an absorption enhancing composition."

The Examiner also again asserts that

> when the species is clearly named, the species claim is anticipated no matter how many other species are additionally named. *Ex Parte A*, 17 USPQ 2d 1716 (Bd. Pat. App. & Int. 1990) (The claimed compounds was named in a reference which also disclosed 45 other compounds. The Board held that the comprehensiveness of the listing did not negate the fact the compound claimed was specifically taught.

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> In the instant case, the species is hydrophilic agents in which simple dissolution is not sufficient to provide efficient absorption of the therapeutic agent.

(*See*, Office Action, pages 8-9). Again, as set forth in the previous Response, mailed April 4, 2008, the above matter is completely different from that in *Ex Parte A*. In *Ex Parte A* Applicant was trying to claim a single compound that was named within a list of compounds in the prior art. Applicants claimed compositions do not involve simply claiming a composition that is recited in a list. Rather, Applicants' discovery is a composition made by forming a salt of a pharmaceutically active compound and a lipophilic counterion and combining the salt with a pharmaceutically acceptable water immiscible solvent to form an injectable composition that, when administered to an animal, forms a depot that releases the active compound over time (claim 1) or is a clear solution that, when injected into water, forms a cohesive oily mass (claim 44). Unlike the matter in *Ex Parte A*, Applicants composition is not a species that has been selected from a list of species in Patel. Patel does not disclose, much less even suggest, the composition claimed in independent claims 1 and 44. Patel merely discloses that using surfactants can enhance absorption of hydrophilic therapeutic agents using various absorption-enhancing components (Patel at column 3, line 51-53 and column 4, line 46-60). The present matter is clearly distinguished from that in *Ex Parte A*.

In summary, Patel does not disclose or suggest a pharmaceutical compositions comprising the components recited in independent claims 1 and 44 or provide any motivation to formulate a composition as recited in independent claims 1 and 44. Moreover, even if there was such a motivation, Patel provides no reasonable expectation that the resulting composition would "when administered to an animal form[ ] a depot that releases the active compound over time " (claim 1) or "when injected into water, form[ ] a cohesive oily mass" (claim 44). Indeed, Patel teaches away from such a composition. Moreover, the claimed compositions, by releasing the active compound over time, advantageously permits administering active compounds to animals that previously could not be widely used because of safety considerations, such as toxicity, as well as requiring less time and resources (Specification at ¶¶ [0015] and [0019], *see also* Example 9, in particular ¶ [0065]). This unexpected advantage is neither disclosed or suggested in Patel.

For the above reasons, Applicants respectfully submit that the compositions recited in

independent claims 1 and 44, as amended, and claims dependent therefrom, are not obvious in view of Patel. Accordingly, Applicants respectfully request that the rejection of claims 1, 3-8, 11, 12, 14, 44, 59-64, 67, 68, and 70 under 35 U.S.C. § 103(a) as being obvious over Patel be reconsidered and withdrawn.

Applicant appreciates the Examiner's recognition that claims 9-10, 13, 65-66, and 69 are not obvious in view of Patel. Claim 9, 13, 65, and 69 were amended to be in independent form. Accordingly, independent claims 9, 13, 65, and 69 and claims 10 and 66, which depend therefrom, respectively, should be allowed after the double patenting rejection, discussed below, is addressed.

**DOUBLE PATENTING**

Claims 1, 3-14, and 59-70 were provisionally rejected on the grounds of non-statutory obviousness-type double patenting as being unpatentable over claims 1-6, 10-12, 17-19, 27-30, and 38-41 of U.S. Patent No. 7,033,599 ("the '599 patent") for the reasons set forth on pages 4-5 of the Office Action.

Claims 1, 3-14, and 59-70 were provisionally rejected on the grounds of non-statutory obviousness-type double patenting as being unpatentable over claims 1-2, 4-10, and 14-19 of U.S. Patent No. 7,404,964 ("the '964 patent") for the reasons set forth on pages 5-6 of the Office Action.

Claims 1, 3-14, and 59-70 were provisionally rejected on the grounds of non-statutory obviousness-type double patenting as being unpatentable over claims 1-11, 13-20, and 32-35 of co-pending U.S. Application Serial No. 10/974,833 ("the '833 application") for the reasons set forth on page 6 of the Office Action.

Claims 1, 3-14, and 59-70 were provisionally rejected on the grounds of non-statutory obviousness-type double patenting as being unpatentable over claims 65-138 of co-pending application serial no. 11/088,922 ("the '992 application") for the reasons set forth on pages 7-8 of the Office Action.

Specifically, the Examiner alleges that claims of the present application are not

patentably distinct from the claims of the '599 patent, the '964 patent, the '833 application, or the '992 application because the instant and conflicting claims recite substantially the same subject matter differing only in the description of the particular components claimed.

Concerning the provisionally rejection of the claims on the grounds of non-statutory obviousness-type double patenting as being unpatentable over certain claims of the '599 patent and the '964 patent, Applicants note that the rejection is provisional. Accordingly, once all rejections of the claims over prior art have been addressed, Applicants will submit a Terminal Disclaimer disclaiming the term of any patent that should issue from the above-identified application that would extend beyond the term of the '599 patent or the '964 patent.

Concerning the provisionally rejection of the claims on the grounds of non-statutory obviousness-type double patenting as being unpatentable over certain claims of the '833 application, Applicants respectfully submits that the rejection is improper. Specifically, the '833 application is not prior art to the above-identified application. The '833 application was filed on October 28, 2004 and claims the benefit of U.S. Provisional Application Serial No. 60/516,967 ("the '967 application"), filed October 29, 2003. The above-identified application, however, was filed on August 27, 2003. Thus, the filing date of the above-identified application predates the filing date of both the '833 application and the '967 application. Accordingly, the '833 application is not prior art to the above-identified application and, therefore, cannot be used to make an obviousness-type double patenting rejection.

Concerning the provisionally rejection of the claims on the grounds of non-statutory obviousness-type double patenting as being unpatentable over certain claims of the '992 application, Applicants note that the '922 application issued as the '964 patent, discussed above. Accordingly, filing a Terminal Disclaimer disclaiming the term of any patent that should issue from the above-identified application that would extend beyond the term of the '964 patent, after all rejections of the claims over prior art have been addressed, will address this rejection. .

Once all rejections of the claims over prior art have been addressed, Applicants will submit a Terminal Disclaimer disclaiming the term of any patent that should issue from the above-identified application that would extend beyond the term of the '599 patent and the '964 patent.

## CONCLUSIONS

It is respectfully submitted that all claims are now in condition for allowance, early notice of which would be appreciated. Should the Examiner disagree, Applicants respectfully request a telephonic or in-person interview with the undersigned attorney to discuss any remaining issues and to expedite eventual allowance of the claims.

Applicant believes a fee of $660.00 is due for the addition of three (3) independent claim in excess of three (3). Please charge this and any other required fees to Townsend and Townsend and Crew LLP deposit account no. 201430.

Respectfully submitted,

Date: October 28, 2008

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